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STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

DATE: **May 15, 2000**

MEMORANDUM

SUBJECT: ***Alkyl dimethyl benzyl ammonium chloride (ADBAC)*** - 2nd Report of the Hazard Identification Assessment Review Committee.

FROM: Timothy F. McMahon, Ph.D. 5/16/00
Risk Assessment and Science Support Branch
Antimicrobials Division (7510C)

THROUGH: Elizabeth Doyle, Co-Chair E.A. Doyle 5/16/00
And
Jess Rowland, Co-Chair 5/15/00
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)

TO: Timothy F. McMahon, Ph.D.
Risk Assessment and Science Support Branch
Antimicrobials Division (7510C)

PC Code: 069105

On February 22, 2000, the Health Effects Division's Hazard Identification Assessment Review Committee met to re-evaluate the Chronic Reference Dose (RfD) for **ADBAC,** at the request of Dr. Timothy McMahon, Antimicrobials Division. A chronic Reference Dose had been established previously for ADBAC in the HIARC meeting of October 28, 1999. New data had been reviewed since that time that was felt to have a potential impact upon the chronic Reference Dose. The HIARC's conclusion regarding re-consideration of the chronic Reference Dose is summarized in this memorandum.

Committee Members in Attendance

Members present were: E. Doyle; J. Rowland; N. Paquette; W. Burnam; P. Hurley; T. Levine; E. Mendez; D. Nixon; and B. Tarplee (Executive Secretary).

Data was presented by Dr. Timothy McMahon of the Antimicrobials Division.

Data Presentation:
and
Report Presentation

Tim McMahon.
Senior Toxicologist
Risk Assessment and Science Support Branch
Antimicrobials Division

I. BACKGROUND

The Health Effects Division's Hazard Identification Assessment Review Committee met on October 28, 1999 in order to establish toxicology endpoints for ADBAC, establish an acute and chronic Reference Dose, and consider the special sensitivity of infants and children as mandated by the Food Quality Protection Act. The committee successfully performed these functions at the October 28, 1999 meeting, but since that time, Dr. McMahon discovered additional Toxicology data on ADBAC in the form of a chronic toxicity study in dogs (MRID # 43221101) that was felt by him to be relevant for establishing the chronic Reference Dose but which had not been included in the original data package to the HIARC.

This memorandum summarizes the deliberations of the HIARC and the conclusions regarding the relevance of the data in the chronic toxicity study in dogs for establishing a chronic Reference Dose for ADBAC.

II. REVIEW OF CHRONIC TOXICITY STUDY IN DOGS

The HIARC considered the data in the chronic toxicity study in dogs, the executive summary of which is presented below:

E.I. Goldenthal (1994): Evaluation of ADBAC in a One-Year Chronic Dietary Study in Dogs. IRDC for ADBAC Quat Joint Venture/ CSMA. Laboratory Project No: 638-004. Study submitted May 3, 1994 under MRID # 43221101.

In a chronic toxicity study in dogs, groups of 4 male and female beagle dogs per group received either 0, 120, 400, or 1200 ppm (0, 3.79, 13.1, or 33.8 mg/kg/day in males and 0, 3.67, 14.6, or 38.6 mg/kg/day in females) alkyl dimethyl benzyl ammonium chloride [ADBAC, 80% a.i.] as a direct dietary admix for one year. Systemic toxicity was observed at 400 ppm and above in female dogs and at 1200 ppm in males as reduced body weight gain (approximately 10% reduction) after 52 weeks of exposure. Food consumption was decreased in the 1200 ppm males and females for the entire study period (approximately 15% reduction in males and 5% reduction in females). Based on the data in this study, the Systemic Toxicity NOAEL was 120 ppm (3.79 mg/kg/day in males, 3.67 mg/kg/day in females) and the LOAEL was 400 ppm (13.1 mg/kg/day in males, 14.6 mg/kg/day in females) based on reduced body weight gain.

II. CONCLUSIONS

The HIARC considered whether the NOAEL from the chronic toxicity study in the dog (3.7 mg/kg/day) should be used to derive a chronic RfD, or whether to retain the existing chronic RfD (0.44 mg/kg/day, based on a NOAEL of 44 mg/kg/day in a two-year carcinogenicity / chronic toxicity study in rats). Due to the lack of statistical significance in body weight decreases, the HIARC concluded that this endpoint is not appropriate for regulatory actions and that the existing RfD thus be retained using the results of the chronic toxicity / carcinogenicity study in the rat.